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Biological
& Medical
Serials

New Series, Vol. II. No. 7.

PROCEEDINGS

OF THE

NEW YORK PATHOLOGICAL SOCIETY

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December, 1902.

PUBLISHED BY THE SOCIETY

August Jerome Lartigau, Editor
437 West 59th Street, New York City

Proceedings
of the
New York Pathological Society.

New Series, Vol. II. DECEMBER, 1902. No. 7

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Dr. James Ewing, *President.*

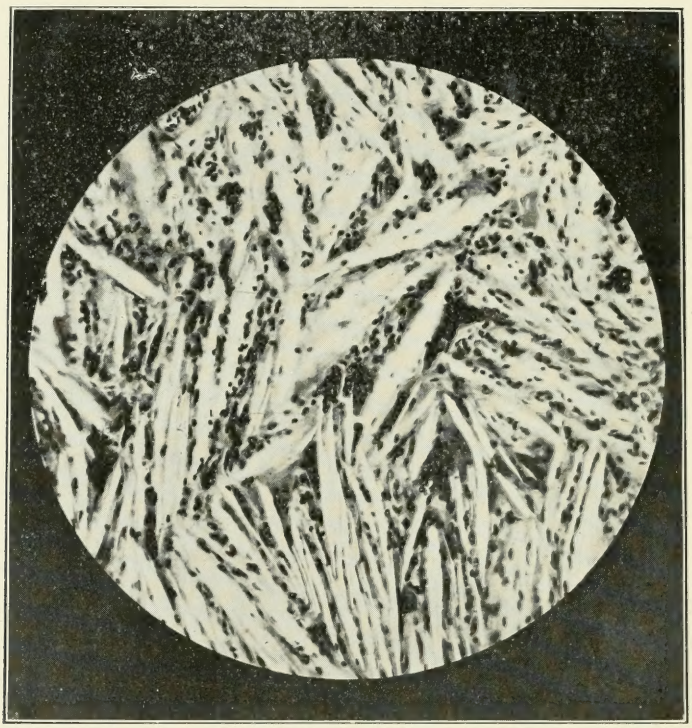
CHOLESTERIN GIANT CELLS.

F. S. MANDLEBAUM, M. D.

In a recent article by Le Count the statement was made that the slits or clefts formed by the solution of cholesterin in granulation and necrotic tissue tumors, formed in the processes of fixation, have frequently been observed and their connection with cholesterin crystals recognized. Le Count says, moreover, that all persons working along general pathological lines are thoroughly familiar with this condition and its occurence is well known to those who make routine examinations of pathological material. In tissue work along these lines during the past twelve years I have met this condition in but two cases and I consequently deem the matter of suffi-

cient importance to bring before the Society. Incidentally I may remark that all the text books with which I am familiar fail to mention this condition.

The first case was that of a woman of thirty years of age who had a small, probably congenital, pre-thyroid cyst. She was operated upon and a small piece of tissue



sent to me for examination. The cyst wall had a granular, honey-combed appearance, and was covered with an exudate, the character of which was not known. Several small openings were seen in the deeper parts which barely admitted the end of a small probe.

The second case was a cyst of the breast in a woman of fifty, who had had the condition for ten years. Re-

cently the cyst began to enlarge and a sinus formed which discharged a thick yellow fluid. The cyst was removed and a portion of it submitted to us. It showed the following gross appearances: From the cyst wall there sprang a rather shaggy, dark reddish colored exudate somewhat granular and friable in character, not very adherent to the cyst wall and easily separated from it and measuring from one-half to one cm. in thickness. The nature of this exudate was not recognized. Sections of this cyst and also of the first case showed the following conditions: The first thing noticeable was a large number of slit-like openings, elliptical in shape, pointed at both ends, and very sharply defined, which looked as though they had been punched out of the tissue with a sharp instrument. The next thing noticeable was the large number of giant cells scattered throughout the whole section. They were of the kind generally seen in inflammatory processes, very large in size and containing thirty or forty nuclei scattered throughout the cell body. They were rich in chromatin and stained very deeply. Within the body of many giant cells these small elliptical slits were also noticed. In some there were two such clefts. The rest of the tissue was made up of inflammatory tissue, vascular and connective tissue. Many of the giant cells contained coarsely granular pigment.

A study of the sections proved that these slit-like openings were produced by cholesterin, which in tissue does not take the tablet form usually seen in fluid exudates, but appears in these elliptical shapes. My impression is that the cholesterin was present in combination with fatty acids. The specimens naturally went through alcohol and ether which extract the cholesterin. This explains why one does not discover the cholesterin crystals themselves which are in the tissue, but simple

the clefts out of which they are extracted. The alcohol is usually thrown away so that chemical tests cannot be made of it. I nevertheless made such tests but did not get any reaction for cholesterin. I then took a bit of tissue from the second case and macerated it with chloroform and from this solution obtained crystals which resembled those of fatty acids. These crystals and also bits of the tissue itself gave reactions for cholesterin. There was the usual play of colors when treated with sulphuric acid and ferric chloride and the violet color remained. One would imagine that these cholesterin crystals ought to present the familiar appearance described; they do not, however, as many complex changes undoubtedly occur, due to various chemical unions.

I have here sections of both cases and also slides showing the fatty acids obtained by evaporating the chloroform in which parts of the specimen had been macerated.

Thoma, in *Virchow's Archiv*, Vol. CV, reports a case of atheroma of the aorta in which these crystals were found. Also Manasse, in Vol. CXXXVI, gives a number of cases of chronic otitis media, several presenting a similar condition. Carl Meyer, (*Ziegler's Beiträge, 1893*, Vol. XIII), reports the case of an adenomatous cyst of the ovary which ruptured intra vitam, in which at operation a large number of miliary nodules were found scattered over the peritoneum. The diagnosis of miliary tuberculosis was made. Upon microscopic examination the nodules were found to be made up of giant cells and cholesterin crystals. The illustrations which accompany the article are identical with the sections in the present cases. Le Count reports a case of carcinoma of the scalp and a case of a tumor mass removed from the scrotum, in both of which specimens of cholesterin giant

cells were found. He also produced similar histological pictures by injecting into the back of a guinea-pig a sterilized salt solution containng pure cholesterin crystals, and by making sections of the nodules which resulted. His article is published in the *Journal of Medical Research*, *1902*, Vol. VII.

Discussion.

Dr. Wood: Has Dr. Mandlebaum made tests on other sections so as to eliminate the possibility of these color reactions having been produced by the action of the strong acid on the proteid of the specimen itself?

Dr. Mandlebaum: I have not made such tests and I do not know whether the ordinary proteid would give that reaction in strong sulphuric acid and whether that obtained could be due to it. I have made other tests with sulphuric acid and the addition of small quantities of iodine and obtained both reactions. I am inclined to believe these were conclusive. I also evaporated the extracted chloroform and so obtained a reaction. It was not quite so marked with nitric acid and ammonia tests.

THE INFLUENCE OF NEPHRECTOMY UPON ABSORPTION.

S. J. MELTZER, M.D., AND WILLIAM SALANT, M.D.

The object of this research, as the title indicates, was to investigate the behavior of absorption after nephrectomy—a subject which was never investigated before. The fact that œdema, which is an accumulation of lymph within the tissue spaces, is found in many cases of

kidney disease, that is, in partial impairment of kidney function, led many writers to the expressed or implied belief that nephrectomy ought to diminish the power of absorption of lymph from the tissue spaces. It must be stated, however, that impaired absorption was left out in the consideration of the well-known theories of œdema. Thus, according to Bright, hydremia is the cause of œdema. Grainger Stewart and Bartels consider hydremic plethora as the cause, while Cohnheim held that increased permeability of the blood vessels brings about this pathological condition. In all of these theories, therefore, increased transudation from the blood vessels into the tissue spaces is considered as the cause of œdema. Not until very recently did it occur to investigators that it might be due also to diminished absorption. As far as we know, Reichel was the first investigator to urge that impaired absorption might account for œdema. He performed a number of experiments on healthy persons and on cases with nephritis or cardiac disease, in whom he injected subcutaneously normal salt solutions. Reichel states that while in the normal individuals the artificial œdema disappeared after two days, it lasted five, eight, and even ten days, in his patients with nephritis or cardiac disease. But Reichel selected cases in which there was no œdema. If his theory be correct, if the formation of œdema be due to impaired absorption, his cases in whom diminished absorption was proved experimentally should have developed œdema. It occured to us that a study of absorption in nephrectomized animals might throw some light on the causation of this pathological condition. Following Reichel's example, we injected subcutaneously into rabbits normal salt solutions, but as absorption by this method could not be studied with any degree of accuracy, our studies were made on absorption from the

peritoneal cavity—a method which is capable of giving more precise results. We began by injecting a 0.8% salt solution which we allowed so remain in the peritoneal cavity for from one-half to nineteen hours. Injection was begun immediately after nephrectomy. Since we know that removal of the kidney leads to plethora and consequent increase of filtration, we expected in common with many others that absorption would be better in normal than in nephrectomized animals. In the first few experiments, however, we obtained entirely different results. Absorption was markedly better in nephrectomized than in normal rabbits. We found that the average per cent of absorption per kilometer of normal rabbits was forty-three per cent, while in the nephrectomized rabbits it was sixty-five per cent.

At this stage of our investigation it occurred to us that there might possibly be a rise of osmotic pressure in the blood of nephrectomized rabbits, for the removal of the kidneys which leads to plethora may likewise cause an accumulation of salts in the blood since the osmotic pressure of the urine is normally higher than that of the blood. If this hypothesis be true, 0.8% sodium chloride is no longer isotonic with the blood of nephrectomized rabbits, but is hypotonic.

With this hypothesis in view, several series of experiments were performed with salt solutions of different concentrations, injecting them immediately after nephrectomy or about twenty to twenty-five hours later. The results are as follows:

One per cent solution injected twelve to twenty-seven hours after double nephrectomy: Remained in the peritoneal cavity one and one-half hours. Two experiments. Absorption in normal rabbits = 18% in one; in the other sixty per cent more was recovered than

was injected: in nephrectomized rabbits, absorption equalled forty-seven per cent and forty-three per cent; or an average of 21% for the normal to 45% for the nephrectomized rabbits. The next series was experimented upon with 1.2% salt solution, which was injected either immediately after double nephrectomy or from seventeen to forty hours later, and was allowed to remain in the peritoneal cavity one-half to six hours. In eight experiments of this series the average of absorption was one-half per cent per kilo of normal rabbit to twenty-five per cent of nephrectomized rabbit. Our assumption that there is a rise of osmotic pressure in nephrectomized rabbits is made still more probable by the results of our series with 1.5% salt solution. In three out of four experiments we recovered from the normal rabbits from ten to twenty per cent more fluid than we injected, while in the nephrectomized rabbits thirty per cent per kilo was absorbed. In our next and last series with 2% salt solution, negative absorption, that is more fluid was recovered than was injected, manifested itself for the first time in nephrectomized rabbits. In two experiments in which the solution remained in the peritoneal cavity for one and a half hours, five per cent more in one, and twelve per cent more in the other were recovered than injected, which is in all probability an indication that 2% salt solution is hypertonic for nephrectomized rabbits. We wish to add that in experiments with a stay of six hours in the peritoneal cavity there was hardly any difference of absorption between normal and nephrectomized rabbits in any of the different series we considered. We obtained similar results with 2%, 0.8% and 1.2% salt solutions which is apparently due to the fact, experimentally proven by Heidenhain and Orlow, Hamburger, and others, that after a longer stay in the peritoneal cavity

liquids, whether hypertonic or hypotonic, become isotonic with the blood. The essential results we obtained are that the power of absorption is considerably increased in nephrectomized rabbits. This holds good for at least twenty-four hours after nephrectomy. We have obtained a positive result in one animal when the fluid was injected forty-one hours after nephrectomy. In another rabbit the results differed and it is impossible to tell whether it was due to the weakened condition of the animal which consequently makes the result obtained under these circumstances doubtful. Our results now explain the fact which has been a puzzle to many experimenters, namely, that no œdema is seen after nephrectomy in animals explain the well known clinical observation of anuria persisting for many days without leading to œdema. The cause of all this is that the first effect of nephrectomy is not an increase of transduation of lymph into the tissue spaces, but an increase of absorption from them.

Discussion.

Dr. Levene: I should like to ask whether Drs. Meltzer and Salant have considered that there was only the one possibility that the increases of osmotic pressure in the blood was the cause of the impairment of absorption after nephrectomy, and if this was the case and since the discovery was so new, whether there had not been some chance to prove that the osmotic pressure of the blood was really so much higher than in normal animals. It seems to me that in advancing such a new theory it would be desirable to corroborate it. The technical methods of determining the osmotic pressure of the blood are are so simple and easy to carry out that I believe this determination should have been made before

such an important conclusion was drawn from the experimental results.

Dr. Meltzer: The experiments were carried out with the idea of demonstrating whether absorption was increased or diminished in nephrectomized animals and the question of the determination of the osmotic pressure of the blood is an entirely secondary matter. Indeed, these determinations have already been made by Koranyi and were published in one of his articles, although as the reference was in a footnote it might easily be overlooked. Indeed, Dr. Salant and myself had not known of it until after we had made some of the experiments. Koranyi states he found a distinct difference in the freezing point of normal and nephrectomized animals. In normal animals the freezing point was 0.56 and in nephrectomized animals, 0.70.

Dr. Levene: I should like to ask if the alterations in the circulation or vasomotor disturbances due to the operative technique might not have caused the increased absorption.

Dr. Meltzer: There was no hyperaemia of the peritoneum after operation. The incisions were made as small as possible and the autopsies showed that there was no peritonitis. Indeed, peritonitis will not favor but rather retard absorption. That there occurs no especial change in the circulation after nephrectomy has been shown long ago by V. Limbeck.

DEMONSTRATIONS OF CULTURES OF THE MENINGOCOCCUS AND MICROCOCCUS CATARRHALIS.

H. L. CELLER, M.D.

During the past five years we have had the oppor-

tunity of investigating at the laboratory of Mt. Sinai Hospital, about twenty cultures of the diplococcus intracellularis of Weichselbaum. A review of the literature on this subject demonstrates that considerable confusion concerning the characteristics of this organism exists. Our results on the other hand, with the exception of slight and unimportant variations, have been constant and agree in all essentials with those of Weichselbaum and his assistants. (Ghon and Albrecht, *Wiener Medizinische Wochenschrift, 1901.*)

Morphologically the meningococcus appears as a diplococcus, the contiguous sides of the individual members being flattened and separated by a fine line of division appearing as an unstained area under the microscope. There is a marked tendency to form tetrads, but the chain formation described by Heubner, Jaeger and others, we have never seen. It is common to find great variations in the size of the individual cocci, large forms appearing next to small ones, especially in older cultures. All of our cultures were invariably decolorized by Gram's solution; we have never met with the non-decolorizing form of Heubner. The organism shows no capsule.

Growth on agar is not constant. Some of the cultures grew upon this medium at first but later lost this power, while others showed a gradually increasing profuse growth and could readily be kept alive by transplanting to fresh tubes at intervals of a few days. The addition of human serum—ascitic, pleural or hydrocele—to the agar always gave better results, but the most luxuriant growth was obtained upon the medium devised by Dr. Libman, serum agar plus glucose (½ to 2%). Maximum growth was obtained with the higher percentage of glucose. With the addition of still higher

percentages of glucose (3, 4, 5%) as well as with the use of lactose of sacharose (2%) the development of the organism was neither furthered nor hindered. On Loeffler's serum there is an abundant growth, but there is no advantage over the serum glucose media just described. On glycerine agar the growth varies, usually only a few fine colonies being obtained; but on the addition of serum the growth is profuse.

In fluid media the organism grows characteristically. The growth begins as a diffuse cloudiness near the surface that after two or three days forms a white scum on the surface. The remainder of the medium is at first clear, later slightly clouded, while at the bottom of the tube there is a floccular sediment. There is considerable difficulty in obtaining growth in this form as the shaking of the tube will prevent the formation of the scum or cause it to break up and fall to the bottom after it has formed

The majority of our cultures have grown slightly in ordinary bouillon with and without the addition of sugar in the form of glucose, lactose, or saccharose. Some, however, have only grown upon the addition of serum; the sugar in these cases having apparently little advantageous effect. There is no gas formation in these media in Smith fermentation tubes in which growth is confined to the bulbs.

In litmus milk we have been able to demonstrate growth. The milk is not coagulated and there is no acidity production. On gelatine there is no growth at room temperature.

On potato the results have varied. Sometimes there is no growth, while at others there is a delicate film on the surface that is seen with difficulty or can only be

demonstrated by spreads made by scraping the surface of the medium.

Anaerobically there is no growth.

Almost identical morphologically with the meningococcus, but differing from it culturally, is another organism found in normal and some in pathological conditions on mucous membranes of the respiratory tract, in the eye, the ear, and occasionally in the urethra. This is the micrococcus catarrhalis of Ghon. Our culture of this coccus, obtained through the courtesy of Dr. Buerger of the German Hospital, was isolated from a throat culture.

In spreads this organism also appears as a diplococcus, with some flattening of the adjacent sides of the individual cocci. It decolorizes with Gram's solution. There is no capsule. In all its characteristics it bears so close a resemblance to the gonococcus that it can be differentiated therefrom under the microscope only with great difficulty. The tetrads formed by meningococcus as well as the large forms already described will sometimes, however, serve to differentiate this from the other two organisms. Further, the individuals of the micrococcus catarrhalis are more nearly oval than those of either the gono- or meningococcus.

On agar the micrococcus catarrhalis grows profusely, even in the first generations, herein differing from both the meningococcus and gonococcus, that show either no growth or very slightly growth on this medium. The use of glycerine or serum agar, Loeffler's serum or Libman's serum media affords no particular advantage. In fluid media the scum formation already described is readily obtained if the cultures are not disturbed. The membrane lacks, however, the homogeneity of that formed by the meningococcus, being composed of dry

granular clumps floating on the surface. In the variation in the cloudiness of the medium as well as in the flocular sediment, the two organisms are identical. There is no gas formation in glucose, lactose, or saccharose bouillon in fermentation tubes; growth is confined to the bulb. Unlike meningococcus, acid production in glucose and saccharose bouillon is demonstrable.

In litmus milk there is growth without coagulation or acidity production. On gelatine there is no growth at room temperature, but Ghon reports slight growth after five or six days under proper thermal conditions. On potato, growth is fairly luxuriant, older cultures appearing yellowish brown; the water remains clear. Anaerobically there is no growth.

On plates the meningococcus and micrococcus catarrhalis are readily differentiated. The superficial colonies of the former are light brown in color; there is no nucleus, but at the center are large clumps that gradually diminish in size toward the periphery. The outer zone is finely granular and paler in color. The edge is sharply defined, circular and regular. There is a very close similarity between these colonies and those of the gonococcus. The colonies of the micrococcus catarrhalis are dark brown in color, lighter at the periphery. The older colonies show a distinct dark nucleus, the remainder of the colony being finely granular. The edge is sharply defined and circular but differs from that of the meningococcus in being irregular as though gnawed. Macroscopically the nucleus of the colonies of micrococcus catarrhalis and the white lacquered surface as compared with the absence of nucleus and the grayish-white surface of meningococcus colonies will serve to distinguish between these two organisms.

A most important means of differentiation is fur-

nished by the nature of the growth both on slants of solid media and on plates. On the former the meningococcus presents a shining greyish moist growth that is viscid, stringy and readily scraped from the surface. The growth of the micrococcus catarrhalis, on the other hand is white, dry, crumbly like mortar, and adheres to the surface of the medium. Sometimes the entire growth may be removed as a membrane. On plates the same differences are seen. The viscidity of the meningococcus colonies stands in marked contrast to the dryness of the colonies of micrococcus catarrhalis, that slide along the surface of the medium without breaking up.

It is impossible to enter here fully into the further questions of the influence of titre on growth, and of pathogenicity. Regarding the latter, our results agree with those of other investigators. Our experiments have been limited to inoculations into white mice, guinea-pigs and rabbits. Subcutaneously both organisms are without effect. In a small proportion of cases intraperitoneal and intrapleural inoculations of either meningococcus or micrococcus catarrhalis in mice and in guinea-pigs have been fatal. Autopsy shows a sero-fibrinous peritoneal and a haemorrhagic pleural exudate. A splenic tumor may or may not be present. All the viscera show hyperaemia and degeneration. The organism may be recovered from the exudates and sometimes from the blood and spleen. The virulence of the micrococcus catarrhalis is far less marked than that of the meningococcus. Larger animals are less susceptible. In rabbits, howeverr, intravenous (Ghon, Weichselbaum) and intracranial (Weichselbaum) inoculations of the meningococcus have proven fatal. Injections into the meninges of goats with the production of meningitis have been successfully

carried out both by Heubner and by Councilman, Mallory and Wright.

REMARKS ON THE MENINGOCOCCUS AND ON ITS RELATIONSHIP TO THE GONOCOCCUS AND MICROCOCCUS CATARRHALIS.

E. LIBMAN, M.D.

In connection with the demonstration by Dr. Celler, I should like to make some remarks on my experience with the meningococcus, particularly with the idea of attempting to throw some light on the questions in dispute. During the past five years I have had the opportunity of studying bacteriologically over one hundred cases of meningitis. In most of these, the fluid obtained by lumbar puncture intra vitam was examined; in a few, examinations were made at autopsy only. In these cases I have had the following results:—

Tubercular cases	44
Streptococcus cases	17
Pneumococcus cases	6
Staphylococcus aureus cases	3
Pseudo-influenza bacillus cases	1
Proteus vulgaris cases	1
Bacillus pyocyaneus cases	1
Diplococcus meningitis cases	20

In a few cases, streptococci and a variety of bacilli were found; the last could not be grown aerobically. I suspect that these were anærobes, particularly as all these cases were secondary to mastoid disease. These cases occurred in all the services of the hospital; a few are cases in the private practice of other physicians and myself. (The larger number of cases due to the meningococcus occured in Dr. Koplik's service.)

I wish now to state our opinions on several mooted

points, based on a study of these cases. I shall be very brief, as I hope to report on these data in full on another occasion.

1. As to the relationship of the pneumococcus and the meningococcus from an epidemological standpoint. All our pneumococcus cases were secondary. Observations recorded in the literature would seem to indicate that the pneumococcus can cause epidemic meningitis. Of course, most of these reports were made at a time when the organisms under discussion were much confused. Further observations are neccessary. It is to be noted that any pathogenic organism may produce a meningitis as the only evidence of a systemic sepsis; and an organism may cause a meningitis by first causing an otitis media or a small area of pneumonia. If the primary disease leads in a short time to a meningeal inflammation, the case clinically corresponds to a primary meningitis. One of our pneumococcus cases was characterized by an acute meningitis following within less than twenty-four hours an apparently mild otitis media without pus production.

2. There are on record descriptions of a number of varieties of the meningococcus (Heubner, Jaeger, and others). Some correspond to what Weichselbaum described. Others differ in holding the Gram stain, in the profuseness of their growth on ordinary agar and bouillon or in their growth on gelatin media, etc. All our cultures corresponded to those described by Weichselbaum. None of them ever showed Gram-positive diplococci. There is a variation in the growth on media not containing serum; but when we obtained growth on these media it was never profuse. We only once obtained a growth (very slight) on gelatin at room temperature, and hardly any or none on potato in the incubator. According to

our experience then, there is but one type of the diplococcus meningitidis in the New York cases of cerebrospinal meningitis. Councilman and Wright found the same in Boston, Osler and Hirsch in Baltimore, and Herrick and others in Chicago. We are inclined to believe that there is but one type of organism at play in the European cases. The description of other varieties we believe to be due to one of three causes:—

a) Variations in the use of the Gram stain;

b) Use of other methods for differential staining. (For instance, Heubner uses a Gram-Weigert stain.)

c. The occurrence of skin contaminations (staphylococci).

3. If it were not for a statement in Leube's book on diagnosis (last edition), it would hardly be necessary to point out that the pneumococcus should not be confused with the meningococcus. Leube says that animal experiments are necessary for the identification of these organisms. However, if it be granted that the meningococcus does not hold the Gram stain we have a fundamental difference. Furthermore, the pneumococcus is lancet-shaped, has a capsule, diffusely clouds bouillon, grows much less profusely than the meningococcus in serum media, etc.

4. As to the occurrence of the meningococcus in the nose and throat, we have made no extensive observations. We found several years ago that other diplococci occur in the nose and throat which resemble the meningococcus morphologically and in staining reactions. In one case, reported by Dr. Koplik in the *Medical News* of last year, Dr. Schwarz found the meningococcus (proven culturally) in a conjunctival inflammation which was followed by a fatal attack of meningitis. The

meningococcus was repeatedly found in the cerebro-spinal fluid.

5. The demonstration of the micrococcus catarrhalis by Dr. Celler I consider of prime importance not only with regard to the undoubted confusion it has caused with regard to the meningococcus, but also because it can be so easily mistaken for the gonococcus if cultures are not made. I have repeatedly seen it in cultures from the throat and in sputum, and once in otitis media. It has been found in the urethra, and probably in the conjunctival sac. The culture of the micrococcus catarrhalis demonstrated to-night corresponds to those which Ghon and Albrecht describe (*Zeitschrift für Klinische Medizin*, Vol. 44). I am convinced that this is but one of a group of closely allied organisms. Dr. Celler has detailed sufficiently how easily it is to be distinguished from the meningococcus.

6. Dr. Celler's remarks have also indicated how the meningococcus can at times closely resemble the gonococcus culturally. It is important to differentiate the organisms carefully. This is true not only from a mere technical standpoint but also because the question may arise clinically. Thus, Fraenkel has described meningococcus-like organisms in conjunctivitis. Furbringer reported a case in which a cerebro-spinal meningitis occurred in a patient with gonorrhoea. The meningococcus was found in the puncture fluid and apparently (cultures not made) the gonococcus in the urethral discharge. Furthermore, there are reported two cases in which the meningococcus was found in the blood; in one, long before symptoms of meningitis were manifest. In such cases as this last, careful methods should be used before the identity of the organism is established. We would lay special stress on these points:—

A. The occurrence of tetrads and the irregularity in size and staining reactions of the meningococcus.

B. The profuse growth of the meningococcus in Loeffler's serum and the absence of any growth of the gonococcus on this medium. Some claim to have seen a slight growth of the gonococcus.

C. We never obtained growths of the gonococcus in agar. At times the meningococcus grows on agar. Some writers have noted slight growths of the gonococcus on agar. In any event a good growth on agar speaks against the gonococcus.

In serum bouillon media and serum glucose bouillon media the two organisms grow practically in the same way. I have repeatedly noted that the growth of the gonococcus in fluid media, if the observations are carefully made, is on top of the fluid in the form of a white scum. This feature of the gonococcus has as far as I have been able to determine never before been described. I hope to go into this subject in a later paper dealing with the biology of the gonococcus.

7. None of the three organisms under discussion causes precipitation in any of my serum sugar media. According to our experience staphylococci always precipitate in two per cent glucose serum agar. By the use of this medium the occurrence of the confusion of staphylococci with meningococci, which Ghon and Albrecht suspected in some of the reported observations, can be avoided.

8. As to the frequency of finding the meningococcus in cases of cerebro spinal meningitis — we have studied thirty cultures in twenty cases—in some, repeated examinations were made. In all the cases we found the diplococci in spreads or in cultures. In the first seven cases we failed to obtain the organism culturally in one.

In the last seventeen cases we always succeeded in obtaining cultural results. These seventeen cases were studied by the aid of the serum glucose media. At times the organisms are found in spreads at first and not later. Cultures may be positive first and negative later. We believe the diagnosis can always be established if the examinations are made early. In cases of long standing, cultures and spreads might be found negative.

Ghon reports twenty-two positive results in thirty cases, (but some fluids were sent from a distance). Osler found the cocci in spreads or in culture, twenty-seven times in thirty cases. Councilman, Mallory and Wright examined puncture fluids in fifty-five cases. The diplococcus was found in spreads or in cultures in thirty-eight. Gradwohl, (St. Louis), describes cultures which can hardly be considered as being those of the meningococcus.

9. We obtained results with small amounts of fluid when we used the two per cent serum glucose agar. We usually poured one-half to one cubic centimetre of fluid into a tube of the medium. Twice a day the condensation fluid and added fluid were allowed to flow over the surface of the medium (Heubner's method). It often required forty-eight hours for a result. Once it required seventy-two hours.

The occurrence of a growth of a Gram-negative diplococcus which shows no or but slight growth on agar, no growth on gelatin nor on potato nor on bouillon in twenty-four hours, which causes no change in litmus milk in the same time, and which grows profusely on Loeffler's medium, is sufficient to make the presence of the meningococcus a certainty.

These final remarks hold true provided media of certain titres are used. From our experiences we would

say that the media not containing serum should be neutral or slightly alkaline to phenolphthalein. The serum media should be made from agar which is one-half or one per cent acid. The subject of titer is of extreme interest with regard to the meningococcus and gonococcus. We hope to report further on this aspect of the subject.

Discussion.

Dr. Brooks: Several years ago I studied a series of cases of purulent meningitis. This was before Dr. Libman's culture media had been devised. I became so mixed up with the various forms of meningococci that I did not dare to publish the results. I have found it very difficult at times to differentiate between the meningococci and the micrococcus catarrhalis. I also found that animal experiments were very uncertain. I also found that large quantities of culture were usually required in order to obtain growth of the meningococcus. I believe that the work of Dr. Libman and Dr. Celler is most important and will be particularly appreciated by those who have done any work with these organisms.

EXPERIMENTS RELATING TO THE FIXATION OF STRYCHNINE BY ANIMAL TISSUES.

G. LANGMANN, M.D., AND S. J. MELTZER, M.D.

While it was formerly supposed that strychnine, whether taken by the mouth or injected hypodermically, combined with the tissue, Dragendorff and other observers proved that it left the system unaltered and was

principally excreted by the kidneys within less than forty-eight hours. Von Czyhlarz and Donath revived this question in 1900 by claiming that strychnine when injected into a ligated extremity of a guinea-pig was neutralized by contact with the living tissues. Repeating the same experiments, we were unable to confirm these statements; we believe it probable that absorption is impaired by the constriction and that sufficient elimination takes places so that at no time an efficient minimum was reached. Carrara, however, sustained the theory of v. Czyhlarz and Donath by apparently conclusive experiments. After checking all elimination through double nephrectomy he found that strychnine injected into a ligated extremity caused no symptoms. Although this premise sounded very plausible it was never tested by experiment. Meltzer and Salvant found that rabbits, at least after double nephrectomy would tolerate the gradual injection of the triple lethal dose without exhibiting the least effect of strychnine. The same experiments were repeated by us on guinea-pigs and it was found again that after double nephrectomy doses far above the lethal may be injected without obtaining a single symptom of strychnine poisoning provided that not too large single doses were used and that they did not follow each other too closely. The gradual injection of as much as twenty mgr. per kilo did not even cause a hyperaesthesia although the lethal dose for normal animals is four mgr. per kilo.

These experiments, therefore, cannot be adduced to sustain von Czyhlarz and Donath's theory. It was furthermore established that strychnine was ineffective provided it was not injected within the first three hours after nephrectomy. Previous to that period even subminimal doses proved fatal. Some of the nephrecto-

mized animals exhibited a *subtetanic reaction*, a peculiar continuous vibration, ending in death within an hour. It seems likely that during the hours following nephrectomy the system elaborated a compensatory mechanism of elimination for the injection of strychnine into a ligated extremity proved to be fatal if nephrectomy was performed and the ligature loosened three hours after the injection.

Discussion.

Dr. Levene: I have made the same observations that Dr. Langmann has made in support of his theory as to the reaction of the organisms on strychnine. A paper has appeared during the year on the antitoxic effect of nerve tissue on tetanus toxin. It is claimed by the author that nerve tissue has not the power to absolutely neutralize tetanus toxin but to a certain extent diminishes its effect. Tetanus toxin was given to an aminal mixed with the pulp of brain tissue. It was found that smaller amounts of antitoxin were needed to save the life of the animal that when the toxin was injected directly without the brain emulsion. This author therefore claimed a specific antitoxic effect for the brain emulsion. It seems to me that the simpler explanation would be that the tetanus toxin acted more slowly in colloidal solution than when injected directly and that therefore less antitoxin was necessary to save the life of the animal.

Dr. Meltzer: I do not arise again to defend my own experiments but those of another. Wasserman's experiments were not performed by mixing brain tissue and tetanus toxin but the toxin was injected into one side of the animal and the brain tissue into the other side.

Dr. Levene: I did not have reference to Wasserman's experiments.

REMARKS ON VASO-MOTOR NERVES, WITH DEMONSTRATIONS.

S. J. MELTZER, M.D., AND CLARA MELTZER, M.D.

Since 1852 the sympathetic has been considered the sole or main vaso-motor nerve of the ear. This is the impression one gets from examining text-books on physiology. We investigated the subject in a series of twenty-one rabbits. Without entering upon a description of the operation the following results may be given: In about one-half of the animals the dilatation of the vessels of the entire ear after section of the third cervical was well marked and as good, if not better than that following section of the sympathetic. In only two, section of the cervical had almost no effect. In the balance the dilatation was chiefly in the vessels of the upper part and sides of the ear. Section of the left cervical gave more distinct effects than that of the right. It seemed that this applied also to the sympathetic. In a number of animals we especially noted that white the effect of the section of the sympathetic is considerably diminished in three or four days, that of the cervical continues in most animals undiminished for a much longer period. We got the impression that the color of the animal had some influence. Stimulation of the peripheral cut end of the cervical also gave in many cases a greater constriction than the stimulation of the sympathetic. In some animals the constriction affected the vessels of the entire ear; in others it affected only the vessels of the top and sides; and in a few there was no effect. In all cases both sides were different, the

left side usually giving greater effects. A few cases were observed in which stimulation of the cervical had very little or no effect; nevertheless section of this nerve caused considerable congestion of the ear which shows that the cervical maintained a vaso-constricting tonus. This means that normal stimuli are more adequate than the artificial ones which we usually employ in experiments. These experiments demonstrate that the blood vessels of the rabbit's ear are under the control of two separate sets of nerves, the cervical and the sympathetic, which can substitute one another—a striking example of collateral innervation.

Discussion.

Dr. Levene: I have been interested in Dr. Meltzer's statement that the color of the animals seemed to have some influence on the results of the experiments. In the work which I have done requiring intravenous injections I always preferred white rabbits. I should like to know whether Dr. Meltzer also found that the vessels of the white rabbit were more developed and whether that explained why the widening after the cutting of the nerve was greater? Was there not a difference between the results of the operation in the right side and on the left side? In nature these arteries are larger on the right side than on the left. Would not the difference in the normal caliber of the arteries on the two sides interfere with the measurements after cutting of the cervical nerves?

Dr. S. J. Meltzer: In regard to the question of the different results according to the color of the rabbit I would not wish to go on record. Hundreds of rabbits would have to be studied before a conclusion in this regard could be positively demonstrated. With regard to Dr.

Levene's second question I may say that the differences between the right and left sides in the widening of the vessels after section of the nerves is not a matter of theory but of observation. We have seen the blood vessels before the section of the nerves and knew that there was no such preformed anatomical differences between the two ears. Nor would this have anything to do with the question of stimualation. By stimulating the nerves on the left side a greater effect is produced than by stimulating those on the right side. This fact has nothing to do with the original size of the vessels.

GLIOMA OF THE BRAIN.

T. C. JANEWAY, M.D.

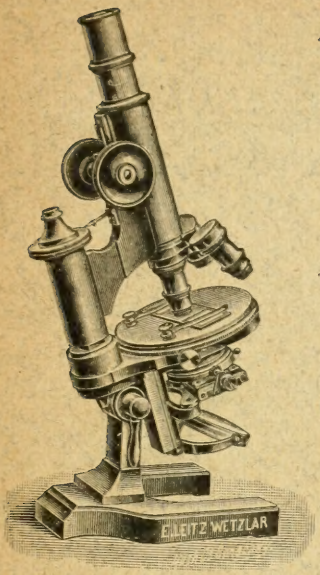
I do not present this specimen because of its remarkable rarity but because the case had a very characteristic history and ran an unusually rapid course. The specimen was obtained from a man of forty who entered St. Vincent's Hospital on the twenty-fifth of October. He gave the following history: He had been a moderate drinker and had chancroids; beyond this there was nothing of any particular importance in his past history. On Labor Day his first symptoms of brain trouble appeared in the form of an attack of dizziness while in a parade. He was compelled to rest and to return home. The same day he travelled to Newburg and while there he fainted and had a repetition of the vertigo. From that time the attacks of vertigo succeeded each other, coming several times a day, and he began to stagger and to run into objects. He had severe headaches which were very much intensified by any movement. The pain

at first was all over the head, but in the latter part of his illness was confined to the right side. He had attacks of vomiting which he referred to taking milk. He was sent to the hospital with a diagnosis of brain fever. On admission he had staggering and exaggerated reflexes, both of the patella and of the arm. The temperature was normal. The right pupil was dilated. Dr. Callan reported optic neuritis which was more pronounced in the right eye. He had perfect control over his bladder and rectum. From that time until December 6, when he died, he was put upon mixed treatment. He was seen by the different attending physicians and by Dr. Starr, and the clinical diagnosis was made of gumma of cerebellum. He improved for a time, but the improvement soon ceased and he became delirious, vomited freely, had intense deadache, and died rather suddenly. At autopsy the following condition was found: He had a fairly marked flattening of the convolutions all over both hemispheres. There was a marked flow of fluid on opening the lateral ventricles. Section of the cortex showed nothing particularly abnormal. On opening the cerebellum in the median line one came upon a small irregular cyst filled with yellowish contents, surrounding which was a narrow area of tissue which was hardly demarcated from the normal white matter of the cerebellum in which it lay except that it seemed to be a little firmer than the rest of the tissue. The lower part involved the right superior peduncle. This portion was in color very much like the normal tissue; there was no distinct line of demarcation. The ragged cyst in the center was filled with yellow contents which showed broken down granular detritus. Sections from the edge showed perfectly typical glioma with very numerous thin-walled blood vessels. Sections from the peduncle showed very cell-

ular glioma with occasional ganglion cells scattered throughout, which were apparently inclusions in the tissue. A point of interest was whether the initial symptom was due to hemorrhage into the solid portion of the tumor and whether the glioma had been of more than two months' duration.

Discussion.

Dr. Brooks: It seems to me rather remarkable from the location of the tumor that it could have existed long before the onset of the first symptoms. I believe that glioma of the brain often develops very rapidly. In my experience glioma of the cerebellum is much rarer than glioma of the cerebrum.



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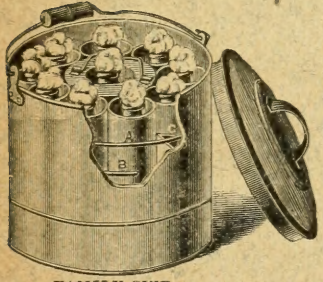
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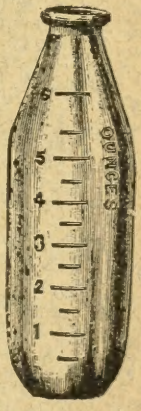

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